CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-564

APPROVAL LETTER

NDA 83-564
AF 9-389

OCT 24 1975

Delco Chemical Company, Inc.
Attention: Louis Cohen
7 MacQuesten Parkway North
Mount Vernon, NY 10550

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delcobese Capsules, 5 mg., 10 mg., 15 mg., and 20 mg.

Reference is also made to your communications dated October 20 and 24, 1975.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.8 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,

Marvin Seife 10/24/75

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

HYC-DD

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-564

APPROVED DRAFT LABELING

DELCOBESE

TABLETS—CAPSULES

(A SINGLE ENTITY AMPHETAMINE PREPARATION)

Supplied in:	5 mg.	10 mg.	15 mg.	20 mg.
Description:				
Dextroamphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Dextroamphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.

AMPHETAMINES HAVE A SIGNIFICANT POTENTIAL FOR ABUSE. IN VIEW OF THEIR LIMITED SHORT-TERM ANORECTIC EFFECT AND RAPID DEVELOPMENT OF TOLERANCE, THEY SHOULD BE USED WITH EXTREME CAUTION AND ONLY FOR LIMITED PERIODS OF TIME IN WEIGHT REDUCTION PROGRAMS.

DESCRIPTION: White, odorless crystalline powders, soluble in water.
DEXTROAMPHETAMINE is the dextrorotary isomer of amphetamine.

ACTIONS: Amphetamines are sympathomimetic amines with CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. The anorectic effect diminishes after a few weeks.

INDICATIONS: Narcolepsy.
Minimal brain dysfunction in children (hyperkinetic behavior disorders), as an aid to general management.
Exogenous obesity, as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncracy to the sympathomimetic amines.
Agitated states.
Patients with a history of drug abuse.
During or within 14 days following the administration of monoamine oxidase inhibitors, hypertensive crises may result.

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.
Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.
Drug Dependence: Amphetamines have a significant potential for abuse. Tolerance and extreme psychological dependence have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.
Usage in Pregnancy: Safe use in pregnancy has not been established. Reproduction studies in mammals at high multiples of the human dose have suggested both an embriotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.
Usage in Children: Amphetamines are not recommended for use as anorectic agents in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.
Insulin requirements in diabetes mellitus may be altered in association with the use of amphetamines and the concomitant dietary regimen.
Amphetamines may decrease the hypotensive effect of guanethidine.
The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS:
Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.
Central nervous system: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely, psychotic episodes at recommended doses.
Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects when amphetamines are used for other than the anorectic effect.
Allergic: Urticaria.
Endocrine: Impotence, changes in libido.

DOSAGE AND ADMINISTRATION: Regardless of indication, amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening medication should be avoided because of the resulting insomnia.
1. Narcolepsy: Usual dose 5 to 60 milligrams per day in divided doses.
2. Minimal brain dysfunction:
   a. Not recommended for children under 3 years of age.
   b. Children from 3 to 5 years of age: 2.5 milligrams daily, raised in increments of 2.5 milligrams at weekly intervals until optimal response is obtained.
   c. Children 6 years of age and older: 5 milligrams once or twice daily, increased in increments of 5 milligrams at weekly intervals. Only in rare cases will it be necessary to exceed a total of 40 milligrams per day.
3. Obesity: Usual adult dose 5 to 30 milligrams per day in divided doses.

OVERDOSAGE: Manifestations of acute overdosage with amphetamines include restlessness, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.
Management of acute amphetamine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

DOSAGE: ADULTS: Tablets or Capsules: One tablet or capsule three times a day ½ hour before meals. Third dose should not be taken after 4 P.M. to avoid insomnia.

CAUTION: FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

Available in bottles of 1,000 and 5,000.

JAN. 1973

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES NDC 697-2530-10

C II

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES NDC 697-2530-51

C II

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	2.5 mg.
Dextroamphetamine Sulfate	2.5 mg.
Amphetamine Adipate	2.5 mg.
Dextroamphetamine Adipate	2.5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES NDC 697-2450-10

DELCOBESE

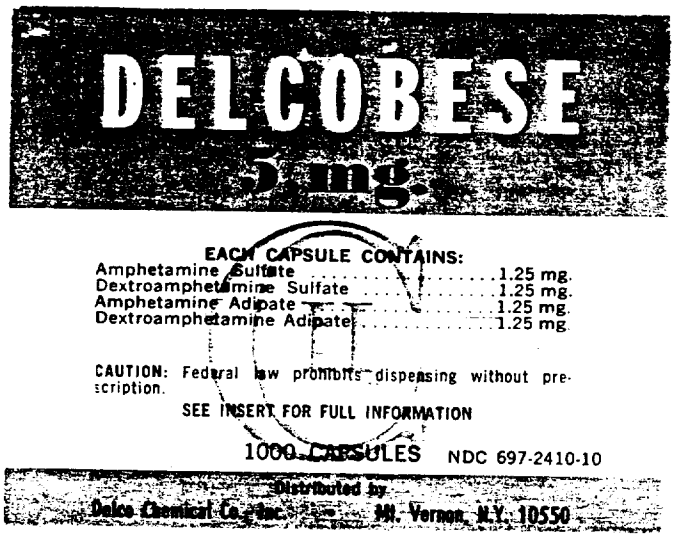
EACH CAPSULE CONTAINS:

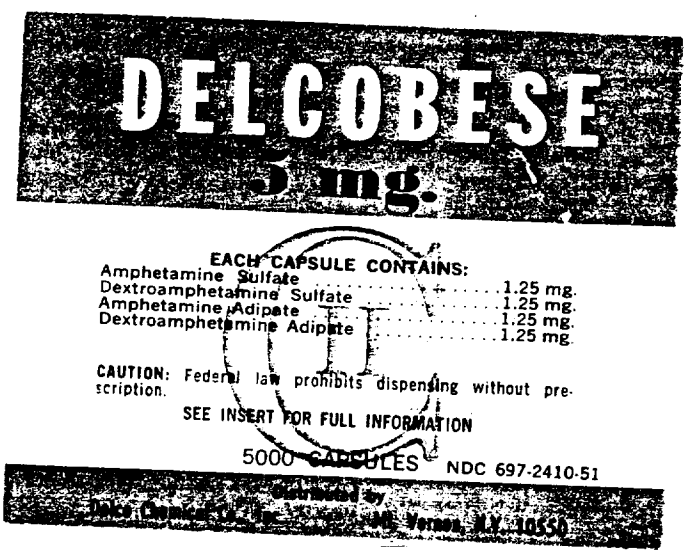
Amphetamine Sulfate	2.5 mg.
Dextroamphetamine Sulfate	2.5 mg.
Amphetamine Adipate	2.5 mg.
Dextroamphetamine Adipate	2.5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

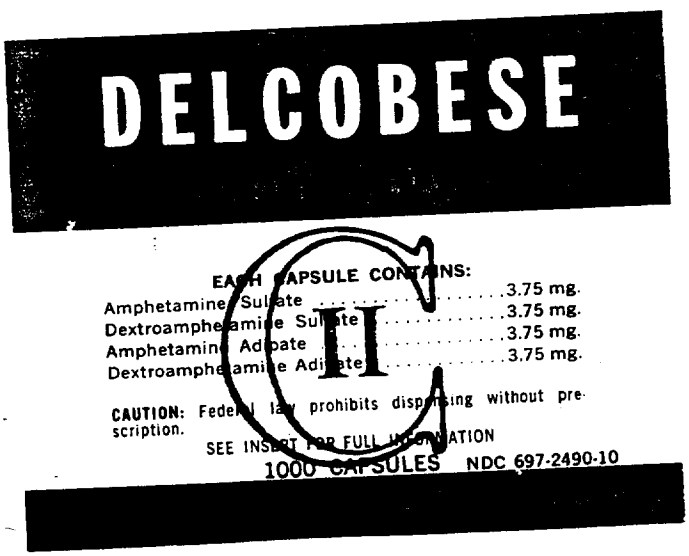
SEE INSERT FOR FULL INFORMATION

5000 CAPSULES NDC 697-2450-51


DELCOBESE
5 mg.
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 1.25 mg.
Dextroamphetamine Sulfate ..... 1.25 mg.
Amphetamine Adipate ..... 1.25 mg.
Dextroamphetamine Adipate ..... 1.25 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
1000 CAPSULES
NDC 697-2410-10
Distributed by
Dolco Chemical Co., Inc.
Mt. Vernon, N.Y. 10550


DELCOBESE
5 mg.
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 1.25 mg.
Dextroamphetamine Sulfate ..... 1.25 mg.
Amphetamine Adipate ..... 1.25 mg.
Dextroamphetamine Adipate ..... 1.25 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
5000 CAPSULES
NDC 697-2410-51
Distributed by
Dolco Chemical Co., Inc.
Mt. Vernon, N.Y. 10550


DELCOBESE
EACH CAPSULE CONTAINS:
Amphetamine Sulfate .....3.75 mg.
Dextroamphetamine Sulfate .....3.75 mg.
Amphetamine Adipate .....3.75 mg.
Dextroamphetamine Adipate .....3.75 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
5000 CAPSULES
NDC 697-2490-51


DELCOBESE
EACH CAPSULE CONTAINS:
Amphetamine Sulfate .....3.75 mg.
Dextroamphetamine Sulfate .....3.75 mg.
Amphetamine Adipate .....3.75 mg.
Dextroamphetamine Adipate .....3.75 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
1000 CAPSULES
NDC 697-2490-10

Labeling: Dup
NDA No. 83-564 Rec'd 12-27-73
Reviewed by

DELCOBESE

TABLETS — CAPSULES

(A SINGLE ENTITY AMPHETAMINE PREPARATION)

Supplied in:	5 mg.	10 mg.	15 mg.	20 mg.
Description:	½			
Dextroamphetamine sulfate .....1.25 mg.	2.5 mg.	3.75 mg.	5 mg.	
Dextroamphetamine adipate .....1.25 mg.	2.5 mg.	3.75 mg.	5 mg.	
Amphetamine adipate .....1.25 mg.	2.5 mg.	3.75 mg.	5 mg.	
Amphetamine sulfate .....1.25 mg.	2.5 mg.	3.75 mg.	5 mg.	

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INDICATIONS: Narcolepsy.
Minimal brain dysfunction in children (hyperkinetic behavior disorders), as an aid to general management.
Exogenous obesity, as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients in whom obesity is refractory to other measures.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncracy to the sympathomimetic amines.
Agitated states.
Patients with a history of drug abuse.
During or within 14 days following the administration of monoamine oxidase inhibitors, hypertensive crises may result.

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.
Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.
Drug Dependence: Amphetamines have a significant potential for abuse. Tolerance and extreme psychological dependence have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.
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CAUTION: FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

Available in bottles of 1,000 and 5,000.

JAN. 1973

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-564

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW FOR ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT	Federal Register Statement Date	ANDA Number 83-563 AF Number 9-389

Name and Address of Applicant (City and State)	Original Amendment xxxxx Supplement Resubmission Correspondance Report Other
Delco Chemical Company, Inc. Mount Vernon, NY 10550	

Purpose of Amendment/Supplement	Date(s) of Submission(s)
modified specifications/tests	10-20-75 10-24-75

Pharmacological Category	Name of Drug	
amphetamine	Delcobese	
Dosage Form(s)	**Potency (ies)**	**How Dispensed**
tablets	5 mg, 10 mg., 15 mg., 20 mg.	R_x xxxxx OTC
Packaging/Sterilization	**Samples**	**Related IND/NDA/MF**
		83-563 tablets 83-564 capsules

Labeling

satisfactory per medical officer's review of 10-23-75

Biologic Availability

not required

Establishment Inspection

satisfactory for inwood-per HFD-322 related memo of 10-21-74

Components, Composition, Manufacturing and Controls

satisfactory

Remarks

approval majarski

M A Jarski 10/24/75

Conclusion

REVIEWED DATE

REVIEW OF RESUBMISSION

DATE COMPLETED: 10-23-73

ANDA #: 83-564

F.R. DATE: 2-12-73

CO. NAME: Delco Chemical Co., Inc.
7 MacQueston Parkway N.
Mt. Vernon, NY 10550

NAME OF DRUG: Trade: Delcobese Capsules, 5 mg., 10 mg., 15 mg., 20 mg.
Generic: Amphetamines
DATE OF SUBMISSION: 8-15-73 Received for review 10-23-73

TYPE OF SUBMISSION: Resubmission

CLINICAL EVALUATION:

1. Review of Studies: For review by the chemist.

2. Review of Labeling:

   a) Container labels: Satisfactory

   b) Package insert: Revise in accord with labeling guidelines including the box warning at the beginning of the insert. Again, we are requesting that the promotional material at the top of the insert listed as "Supplied In" must be labeled How Supplied and placed in the proper format as stated in CFR 3.74 i.e. at the end of the insert.

CONCLUSION:
1. The container labels are acceptable.
2. The package insert must be revised as noted above before approval can be granted.

RECOMMENDATIONS: The company is to be so notified.

J.K Carr

J.R. Carr, D.D.S.

CHEMIST'S REVIEW FOR ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT

Federal Register Statement Date

NDA Number 83-564

AF Number

Name and Address of Applicant (City and State)
Delco Chemical Company, Inc.
Mount Vernon, NY 10550

Original
Amendment
Supplement xxxxx
Resubmission
Correspondance
Report
Other

Purpose of Amendment/Supplement
updating of Inwood SOP
stability data for capsules - product carries a 3 yr. expiration date

Date(s) of Submission(s)
11-14-75

Pharmacological Category	Name of Drug	How Dispensed
amphetamine	delcobese	R_x xxxxx OTC
Dosage Form(s)	Potency (ies)	Related IND/NDA/MF
capsule	see PI sheet	83-563 tablets 83-564 capsules
Packaging/Sterilization	Samples	

Labeling

Biologic Availability

Establishment Inspection

Components, Composition, Manufacturing and Controls

Remarks Note: all enclosures in 83-563

approval majarski

majarski 12/16/75

Conclusion

REVIEWER DATE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-564

ADMINISTRATIVE DOCUMENTS

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 83-563

DATE APPROVAL LETTER ISSUED: 24 OCT 1975

TO: Press Relations Staff *(PA-40)*

FROM:
- [X] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered below.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [X] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

Abbreviated

CATEGORY
- [X] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG

Delcobese

DOSAGE FORM

Tablet

HOW DISPENSED
- [X] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

NAME OF APPLICANT *(Include City and State)*

Delco Chemical Co., Inc.
Mt. Vernon, NY 10550

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

amphetamine

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR:

FORM PREPARED BY

NAME: mc jarski — DATE:

FORM APPROVED BY

NAME: ilmeyer — DATE:

Form FD 1642 (4/73)

PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

REVIEW OF ANDA AMENDMENT

Date Completed: 10/23/75

ANDA #: 83-564 (Capsules)
~~83-563~~ (Tablets)

F.R. Date: 2/12/73

Co. Name: Delco Chemical Company, Inc.
7 MacQuesten Parkway North
Mt. Vernon, NY 10550

NAME OF DRUG: Trade & Generic: Delcobese Tablets, Capsules 5 mg., 10 mg., 15 mg., 20 mg.

5 mg. cpasules 10 mg. caps. 15 mg. 20 mg.

DATE OF SUBMISSION: April 14, 1975

TYPE OF SUBMISSION: Amendment

CLINICAL EVALUATION:

1. Review of Studies: Chemistry and manufacturing data will be reviewed by the chemist.

2. Review of Labeling:
   a. Core item - designation clearly printed on all the immediate container labels, as well as on the package insert.
   b. Immediate container labels are satisfactory; different colors are used for different dosage labels.
   c. Package insert: satisfactory.

CONCLUSION: 1. The immediate container labels and package insert are approved.
2. The manufacturing data will be reviewed by the chemist.

RECOMMENDATIONS: Approval, provided manufacturing data is acceptable.

Marvin Seife

Marvin Seife, M.D.

/75

REVIEW OF ANDA

Date Completed: 4/30/73

ANDA #: 83-564
F.R. Date: 2/12/73
Co. Name: Delco Chemical Co., Inc.
7 N. Macquesten Parkway
Mt. Vernon, N.Y. 10550

NAME OF DRUG: Trade: Delcobese Capsules 5, mg., 10 mg., 15 mg., 20 mg.

Generic: Amphetamines

DATE OF SUBMISSION: 4/6/73

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Studies: None submitted. Bioavailability requirement is currently deferred for conventional dosage form.

2. Review of Labeling:
   a. Container Label: Delete the promotional phrases, "Central Stimulant-Short Term Appetite Depressant."

   b. Package Insert:
   Remove the "Supplied in" data under the name of the drug at the top of the insert and place it as "How Supplied" after over-dosage at the end of the insert. Revise the package insert to conform to current labeling guidelines.

CONCLUSION:

1. Revise the container label as noted above.

2. Revise the package insert as noted above.

RECOMMENDATIONS:
The company is to be notified of the aforementioned conclusion and sent a copy of the labeling guidelines.

J. R. Carr, D.D.S.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

Form Approved
Budget Bureau No. 85-R0045

NEW DRUG APPLICATION *(DRUGS FOR HUMAN USE)*

(Title 21, Code of Federal Regulations, § 130.4)

Name of applicant **DELCO CHEMICAL CO., INC.**

Address **7 N. MACQUESTEN PARKWAY, MT. VERNON, N.Y. 10550**

Date **FEBRUARY 23, 1973**

Name of new drug **DELCOBESE CAPSULES 5 mg. - 10 mg. - 15 mg. - 20 mg.**

[X] Original application (regulation §130.4).
[ ] Amendment to original, unapproved application (regulation §130.7).
[ ] Supplement to an approved application (regulation §130.9).
[ ] Amendment to supplement to an approved application.

The undersigned submits this application for a new drug pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act. It is understood that when this application is approved, the labeling and advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application; and if the article is a prescription drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the drug will contain the same information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant warnings, hazards, contraindications, side effects, and precautions, as that contained in the labeling which is part of this application in accord with §1.106(b) (21 CFR 1.106(b)). It is understood that all representations in this application apply to the drug produced until an approved supplement to the application provides for a change or the change is made in conformance with other provisions of §130.9 of the new-drug regulations.

Attached hereto, submitted in the form described in §130.4(e) of the new-drug regulations, and constituting a part of this application are the following:

1. Table of contents. The table of contents should specify the volume number and the page number in which the complete and detailed item is located and the volume number and the page number in which the summary of that item is located (if any).

2. Summary. A summary demonstrating that the application is well-organized, adequately tabulated, statistically analyzed (where appropriate), and coherent and that it presents a sound basis for the approval requested. The summary should include the following information: (In lieu of the outline described below and the evaluation described in Item 3, an expanded summary and evaluation as outlined in §130.4(d) of the new-drug regulations may be submitted to facilitate the review of this application.)

a. Chemistry.

i. Chemical structural formula or description for any new-drug substance.

ii. Relationship to other chemically or pharmacologically related drugs.

iii. Description of dosage form and quantitative composition.

b. Scientific rationale and purpose the drug is to serve.

c. Reference number of the investigational drug notice(s) under which this drug was investigated and of any notice, new-drug application, or master file of which any contents are being incorporated by reference to support this application.

d. Preclinical studies. (Present all findings including all adverse experiences which may be interpreted as incidental or not drug-related. Refer to date and page number of the investigational drug notice(s) or the volume and page number of this application where complete data and reports appear.)

i. Pharmacology (pharmacodynamics, endocrinology, metabolism, etc.).

ii. Toxicology and pathology: Acute toxicity studies; subacute and chronic toxicity studies; reproduction and teratology studies; miscellaneous studies.

e. Clinical studies. (All material should refer specifically to each clinical investigator and to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found.)

i. Special studies not described elsewhere.

ii. Dose-range studies.

iii. Controlled clinical studies.

iv. Other clinical studies (for example, uncontrolled or incompletely controlled studies).

v. Clinical laboratory studies related to effectiveness.

vi. Clinical laboratory studies related to safety.

vii. Summary of literature and unpublished reports available to the applicant.

3. Evaluation of safety and effectiveness. a. Summarize separately the favorable and unfavorable evidence for each claim in the package labeling. Include references to the volume and page number in the application and in any documents incorporated by reference where the complete data and reports may be found.

b. Include tabulation of all side effects or adverse experience, by age, sex, and dosage formulation, whether or not considered to be significant, showing whether administration of the drug was stopped and showing the investigator's name with a reference to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found. Indicate those side effects or adverse experiences considered to be drug-related.

4. Copies of the label and all other labeling to be used for the drug (a total of 12 copies if in final printed form, 4 copies if in draft form):

a. Each label, or other labeling, should be clearly identified to show its position on, or the manner in which it accompanies, the market package.

b. If the drug is to be offered over the counter, labeling on or within the retail package should include adequate directions for use by the layman under all the conditions for which the drug is intended for lay use or is to be prescribed, recommended, or suggested in any labeling or advertising sponsored by or on behalf of the applicant and directed to the layman. If the drug is intended or offered for uses under the professional supervision of a practitioner licensed by law to administer it, the application should also contain labeling that includes adequate information for all such uses, including all the purposes for which the over-the-counter drug is to be advertised to, or represented for use by, physicians.

c. If the drug is limited in its labeling to use under the professional supervision of a practitioner licensed by law to administer it, its labeling should bear information for use under which such practitioners can use the drug for the purposes for which it is intended, including all the purposes for which it is to be advertised or represented, in accord with §1.106(b) (21 CFR 1.106(b)). The application should include any labeling for the drug intended to be made available to the layman.

d. If no established name exists for a new-drug substance, the application shall propose a nonproprietary name for use as the established name for the substance.

e. Typewritten or other draft labeling copy may be submitted for preliminary consideration of an application. An application will not ordinarily be approved prior to the submission of the final printed label and labeling of the drug.

f. No application may be approved if the labeling is false or misleading in any particular.

(When mailing pieces, any other labeling, or advertising copy are devised for promotion of the new drug, samples shall be submitted at the time of initial dissemination of such labeling and at the time of initial placement of any such advertising for a prescription drug (see §130.13 of the new-drug regulations). Approval of a supplemental new-drug application is required prior to use of any promotional claims not covered by the approved application.)

5. A statement as to whether the drug is (or is not) limited in its labeling and by this application to use under the professional supervision of a practitioner licensed by law to administer it.

6. A full list of the articles used as components of the drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new-drug substance, and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each substance should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

7. A full statement of the composition of the drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug in the form in which it is to be distributed (for example, amount per tablet or per milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variations may be specified.

8. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug. Included in this description should be full information with respect to any new substance and to the new-drug dosage form, as follows in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the drug:

a. A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

b. A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the drug has the safety, identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

c. The methods used in the synthesis, extraction, isolation, or purification of any new-drug substance. When the specifications and controls applied to such substance are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperatures, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the substance may be specified.

d. Precautions to assure proper identity, strength, quality, and purity of the raw materials, whether active or not, including the specifications for acceptance and methods of testing for each lot of raw material.

e. Whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

f. If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new-drug substance or the new-drug dosage form, his statement identifying each person who will perform any part of such operations and designating the part; and a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls in his part of the operation.

g. Method of preparation of the master formula records and individual batch records and manner in which these records are used.

h. The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new drug, including any special precautions observed in the operations.

i. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

j. Number of individuals checking weight or volume of each individual ingredient entering into each batch of the drug.

k. Whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

l. Precautions to check the actual package yield produced from a batch of the drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in event of an unexplained discrepancy.

m. Precautions to assure that each lot of the drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

n. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

o. An explanation of the exact significance of the batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug, including the control numbers that appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

p. A complete description of, and data derived from, studies of the stability of the drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies underway or contemplated. Stability data should be submitted for any new-drug substance, for the finished dosage form of the drug in the container in which it is to be marketed, including any proposed multiple-dose container, and if it is to be put into solution at the time of dispensing, for the solution prepared as directed. State the expiration date(s) that will be used on the label to preserve the identity, strength, quality, and purity of the drug until it is used. (If no expiration date is proposed, the applicant must justify its absence.)

q. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product.

(An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.)

9. Samples of the drug and articles used as components, as follows: a. The following samples shall be submitted with the application or as soon thereafter as they become available. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays:

i. A representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations and a representative sample or samples of each new-drug substance, as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

ii. A representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing and, if any such sample is not from a commercial-scale production batch, such a sample from a representative commercial-scale production batch; and a representative sample or samples of each new-drug substance as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

iii. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new-drug substance and other assayed components of the finished drug: *Provided, however,* That samples of reference standards recognized in the official U.S. Pharmacopeia or The National Formulary need not be submitted unless requested.

b. Additional samples shall be submitted on request.

c. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new-drug application to which it relates.

d. There shall be included a full list of the samples submitted pursuant to Item 9a; a statement of the additional samples that will be submitted as soon as available; and, with respect to each sample submitted, full information with respect to its identity, the origin of any new-drug substance contained therein (including in the case of new-drug substances, a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays. Include for any reference standard a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reported results shall be submitted.

e. The requirements of Item 9a may be waived in whole or in part on request of the applicant or otherwise when any such samples are not necessary.

f. If samples of the drug are sent under separate cover, they should be addressed to the attention of the Bureau of Medicine and identified on the outside of the shipping carton with the name of the applicant and the name of the drug as shown on the application.

10. Full reports of preclinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate preclinical tests by all methods reasonably applicable to a determination of the safety and effectiveness of the drug under the conditions of use suggested in the proposed labeling.

b. Detailed reports of the preclinical investigations, including all studies made on laboratory animals, the methods used, and the results obtained, should be clearly set forth. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the underlying data are available for inspection. The animal studies may not be considered adequate unless they give proper attention to the conditions of use recommended in the proposed labeling for the drug such as, for example, whether the drug is for short- or long-term administration or whether it is to be used in infants, children, pregnant women, or women of child-bearing potential.

c. Detailed reports of any pertinent microbiological and *in vitro* studies.

d. Summarize and provide a list of literature references (if available) to all other preclinical information known to the applicant, whether published or unpublished, that is pertinent to an evaluation of the safety or effectiveness of the drug.

11. List of investigators. a. A complete list of all investigators supplied with the drug including the name and post office address of each investigator and, following each name, the volume and page references to the investigator's report(s) in this application and in any documents incorporated by reference, or the explanation of the omission of any reports.

b. The unexplained omission of any reports of investigations made with the new drug by the applicant, or

submitted to him by an investigator, or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources, whether or not it would bias an evaluation of the safety of the drug or its effectiveness in use, may constitute grounds for the refusal or withdrawal of the approval of an application.

12. Full reports of clinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the drug is safe and effective for use as suggested in the labeling.

b. An application may be refused unless it includes substantial evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

c. Reports of all clinical tests sponsored by the applicant or received or otherwise obtained by the applicant should be attached. These reports should include adequate information concerning each subject treated with the drug or employed as a control, including age, sex, conditions treated, dosage, frequency of administration of the drug, results of all relevant clinical observations and laboratory examinations made, full information concerning any other treatment given previously or concurrently, and a full statement of adverse effects and useful results observed, together with an opinion as to whether such effects or results are attributable to the drug under investigation and a statement of where the underlying data are available for inspection. Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. An application for a combination drug may be refused unless there is substantial evidence that each ingredient designated as active makes a contribution to the total effect claimed for the drug combination. Except when the disease for which the drug is being tested occurs with such infrequency in the United States as to make testing impractical, some of the investigations should be performed by competent investigators within the United States.

d. Attach as a separate section a completed Fo FD-1639, Drug Experience Report (obtainable, with structions, on request from the Department of HEW, F and Drug Administration, Bureau of Drugs *(BD-200)* Rockville, Maryland 20852), for each adverse experience or, if feasible, for each subject or patient experiencing one or more adverse effects, described in Item 12c, whether or not full information is available. Form FD-1639 should be prepared by the applicant if the adverse experience was not reported in such form by the investigator. The Drug Experience Report should be cross-referenced to any narrative description included in Item 12c.

e. All information pertinent to an evaluation of the safety and effectiveness of the drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commerical marketing (for example, outside the United States), or reports in the scientific literature, involving the drug that is the subject of the application and related drugs. An adequate summary may be acceptable in lieu of a reprint of a published report which only supports other data submitted. Reprints are not required of reports in designated journals, listed in §130.38 of the new-drug regulations, about related drugs; a bibliography will suffice. Include any evaluation of the safety or effectiveness of the drug that has been made by the applicant's medical department, expert committee, or consultants.

f. If the drug is a combination of previously investigated or marketed drugs, an adequate summary of preexisting information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted by the applicant to the Food and Drug Administration.

g. The complete composition and/or method of manufacture of the new drug used in each submitted report of investigation should be shown to the extent necessary to establish its identity, strength, quality, and purity if it differs from the description in Item 6, 7, or 8 of the application.

13. If this is a supplemental application, full information on each proposed change concerning any statement made in the approved application.
Observe the provisions of §130.9 of the new-drug regulations concerning supplemental applications.

DELCO CHEMICAL CO., INC.
(Applicant)

Per Louis Cohen
(Responsible official or agent)

PRESIDENT
(Indicate authority)

(Warning: A willfully false statement is a criminal offense. U.S.C. Title 18, sec. 1001.)

NOTE: This application must be signed by the applicant or by an authorized attorney, agent, or official. If the applic or such authorized representative does not reside or have a place of business within the United States, the application m also furnish the name and post office address of and must be countersigned by an authorized attorney, agent, or official resi ing or maintaining a place of business within the United States.

ABBREVIATED
NEW DRUG APPLICATION

Delco CHEMICAL COMPANY, INC.

Specializing In Obesity Products For Over 25 Years

7 MacQUESTEN PARKWAY NORTH • MOUNT VERNON, NEW YORK 10550 • MOunt Vernon 4-8348

83-564

February 21, 1973

Barrett Scoville, M.D., Deputy Director
Division Neuropharmacological Drug Products
Office of Scientific Evaluation,
Bureau of Drugs
Food and Drug Administration
Department Health, Education & Welfare
5600 Fishers Lane
Rockville, Maryland 20852

Ref: Abbreviated New Drug Application
F.R. Vol. 38, No. 28 - February 12, 1973
For: DELCOBESE CAPSULES 5mg., 10mg., 15mg., 20mg.
"A Single Entity Amphetamine Preparation"

Dear Doctor Scoville;

Pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act we are hereby submitting:

a) Form 356-H
b) Volume No. 1 Copy No. 1 (Blue Folder)
c) Volume No. 1 Copy No. 2 (Red Folder)
d) Volume No. 1 Copy No. 3 (Yellow Folder)
e) Eight (8) sets of labels (Unbound)

Respectfully submitted,

DELCO CHEMICAL COMPANY, INC.

Louis Cohen

Louis Cohen, President

RECEIVED
MAR 5 1973
BUREAU OF DRUGS

LC/gf

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 33-564

DATE APPROVAL LETTER ISSUED: DEC 17 1975

TO: Press Relations Staff (HFI-40)

FROM:
- [XX] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

Approved

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [ ] ABBREVIATED ORIGINAL NDA
- [XX] SUPPLEMENT TO ANDA

CATEGORY
- [XX] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG

Delcobese

DOSAGE FORM

Capsule

HOW DISPENSED
- [XX] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

5 mg. 10 mg.

mg.

NAME OF APPLICANT *(Include City and State)*

Delco Chemical Co., Inc.
Mt. Vernon, NY 10550

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

amphetamine

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

control revisions

FORM PREPARED BY

NAME: majarski DATE:

FORM APPROVED BY

NAME: jlmeyer DATE:

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

TRANSMITTAL OF PERIODIC REPORTS FOR DRUGS FOR HUMAN USE
(21 CFR 310.300, 310.302, and 431.60)

DATE SUBMITTED: May 24, 1976

Form Approved OMB No. 57-R0035

INSTRUCTIONS

Submit a separate form *(parts 1 through 4-carbons intact)* for each NDA or Antibiotic Application for which the periodic report contains required reporting information. Attach two copies of report to the form.

Where the same item of information applies to more than one NDA or Antibiotic Application for preparations containing a common active ingredient, that information may be submitted as part of the report for only one such application provided all application numbers to which that part of the report applies are listed in Item 7 and provided a separate form, with duplicate copies of all other required information, is submitted for each number.

Forward form and attachments to Department of Health, Education, and Welfare, Food and Drug Administration *(HFD-106)*, 5600 Fishers Lane, Rockville, Maryland 20852.

1. NDA OR ANDA NUMBER: N 8 3 5 6 4

2. REPORT NO. *(FDA Complete)*: R- 0 1

APPLICANT NOTE

Reference NDA and R numbers *(entered on Acknowledgment Copy)* in any subsequent correspondence regarding report.

3. CFR SECTION NUMBER *(Antibiotic only)*:

4. APPLICANT: DELCO CHEMICAL COMPANY, INC.

5. DRUG NAME: DELCOBESE CAPSULES, 5mg., 10mg., 15., 20mg.

6. TYPE OF REPORT *(Check one (10))*: [X] QUARTERLY [ ] SEMIANNUAL [ ] ANNUAL [ ] OTHER

7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS *(List all numbers if any part of report applies to more than one number.)*

8. PERIOD COVERED BY REPORT

FROM (11-14)		TO (15-18)	
YEAR	MONTH	YEAR	MONTH
1976	Feb. 1	1976	Apr. 30

9. REPORT INFORMATION REQUIRED *(See §§ 310.300(a) or 431.60(a) for description)*
(Enter an "X" in Column A if you have nothing to report. Enter identification of type of information attached in Column C.)
(ALWAYS INCLUDE INFORMATION REQUIRED UNDER "f" AND "g".)

NONE A	TYPE OF INFORMATION B	IDENTIFICATION *(Volume No.(s)/Tab(s)/Page(s) of Report)*
(19) X	a. CLINICAL DATA	NOTED: NO MEDICAL REVIEW INDICATED SIG: R Carr DATE: 6/7/76
(20) X	b. ADVERSE REACTION(S)	5mg. Capsules - 64 x 1M ; 35 x 5M
(21) X	c. ANIMAL DATA	10mg. Capsules -173 x 1M ;139 x 5M
(22) X	d. CHEMICAL OR PHYSICAL DRUG PROPERTIES	15mg. Capsules -547 x 1M ;184 x 5M
(23) X	e. MANUFACTURING OR CONTROL CHANGES (§§ 314.8 (a) (5))	20mg. Capsules- 152 x 1M ;248 x 5M
	f. CURRENT PACKAGE LABELING *(Whether or not previously submitted)*	see attached
	g. QUANTITY DISTRIBUTED	see above

Submission Voted
No Action Indicated
M Jarosko 6/10/76

TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT

Louis Cohen, President

SIGNATURE: Louis Cohen

APPLICANTS RETURN ADDRESS *(Type within the window envelope tic marks)*

DELCO CHEMICAL COMPANY, INC.
7 MacQuesten Parkway North
Mt. Vernon, New York 10550

FDA USE ONLY

10. DATE OF RECEIPT: 76 06 01

11. REPORT FILED IN NDA NO.: N 8 3 5 6 4

12. DIV CODE (78):

13. TYPE CARD (80): S

14. FDA ACKNOWLEDGMENT

RECEIVED
JUN 01 1976
BUREAU OF DRUGS

ORIGINAL

FORM FD 2252 (11-74)

DELCOBESE

(A SINGLE ENTITY AMPHETAMINE PREPARATION)

Amphetamines have a high potential for abuse. They should thus be tried only in weight reduction programs for patients in whom alternative therapy has been ineffective. Administration of amphetamines for prolonged period of time in obesity may lead to drug dependence and must be avoided. Particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic use or distribution to others, and the drugs should be prescribed or dispensed sparingly.

Description: Delcobese is a Single entity amphetamine preparation containing the dextro and dextrolaevo isomers of Amphetamine Adipate and Amphetamine Sulfate.

Actions: Amphetamines are sympathomimetic amines wtih CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects, may be involved, for example.

Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short-term clinical trials.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The origins of the increased weight loss due to the various possible drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS

Narcolepsy

Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social).

Special Diagnostic Considerations:

Special etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

The characteristic signs most often observed are chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG. Learning disabilities may or may not be present. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs.

Drug treatment is not indicated for all children with MBD. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

Drug treatment is not intended for use in the child whose hyperactivity is due to environmental factors and/or primary psychiatric disorders.

Exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction, for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines (see ACTIONS) should be weighed against possible risks inherent in use of the drug, such as those described below.

CONTRAINDICATIONS

Advance arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states..

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS

When tolerance to the "anorectic" effect develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: Amphetamines have been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are alsc noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Reproduction studies in mammals at high multiples of the human dose have suggested both an embryotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: Amphetamines are not recommended for use as anorectic agents in children under 12 years of age.

SEE OTHER SIDE

PRECAUTIONS

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of amphetamines and the concomitant dietary regimen.

Amphetamines may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.

Central nervous system: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely, psychotic episodes at recommended doses.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects when amphetamines are used for other than the anorectic effect.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DOSAGE AND ADMINISTRATION

Regardless of indication, amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening medication should be avoided because of the resulting insomnia.

1. **Narcolepsy:** Usual dose 5 to 60 milligrams per day in divided doses.
2. **Minimal brain dysfunction:**
   a. Not recommended for children under 3 years of age.
   b. Children from 3 to 5 years of age: 2.5 milligrams daily, raised in increments of 2.5 milligrams at weekly intervals until optimal response is obtained.
   c. Children 6 years of age and older: 5 milligrams once or twice daily, increased in increments of 5 miligrams at weekly intervals. Only in rare cases will it be necessary to exceed a total of 40 milligrams per day.
3. **Obesity:** Usual adult dose 5 to 30 miligrams per day in divided doses.

OVERDOSAGE

Manifestations of acute overdosage with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states.

Fatigue and depression usually follow the central stimulation.

Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute amphetamine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Acidification of the urine increases amphetamine excretion. Intravenous phentolamine (Regitine) has been suggested for possible acute, severe hypertension, if this complicates amphetamine overdosage.

DOSAGE: ADULTS: Tablets or Capsules: One tablet or capsule three times a day ½ hour before meals. Third dose should be taken at 4 P.M. to avoid insomnia.

HOW SUPPLIED

Available in tablets and capsules for immediate release.

Description:	**DELCOBESE** for immediate release			
	5 mg.	**10 mg.**	**15 mg.**	**20 mg.**
Dextroamphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Dextroamphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.

In bottles of 1000's and tins of 5000's.

CAUTION: Federal Law Prohibits Dispensing without Prescription.

NDC 697-2410-10

DELCOBESE

5 mg.

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	1.25 mg.
Dextroamphetamine Sulfate	1.25 mg.
Amphetamine Adipate	1.25 mg.
Dextroamphetamine Adipate	1.25 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

Distributed by
Delco Chemical Co., Inc. • Mt. Vernon, N.Y. 10550

NDC 697-2410-50

DELCOBESE

5 mg.

EACH CAPSULE CONTAINS:

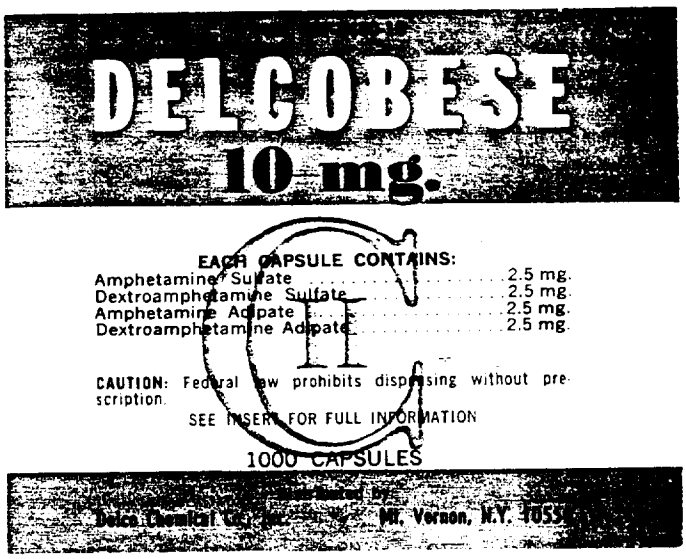
Amphetamine Sulfate	1.25 mg.
Dextroamphetamine Sulfate	1.25 mg.
Amphetamine Adipate	1.25 mg.
Dextroamphetamine Adipate	1.25 mg.

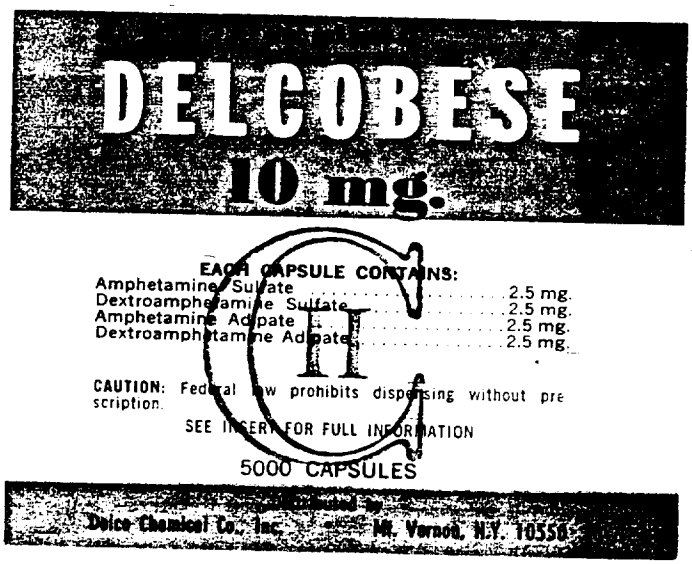
CAUTION: Federal law prohibits dispensing without prescription.

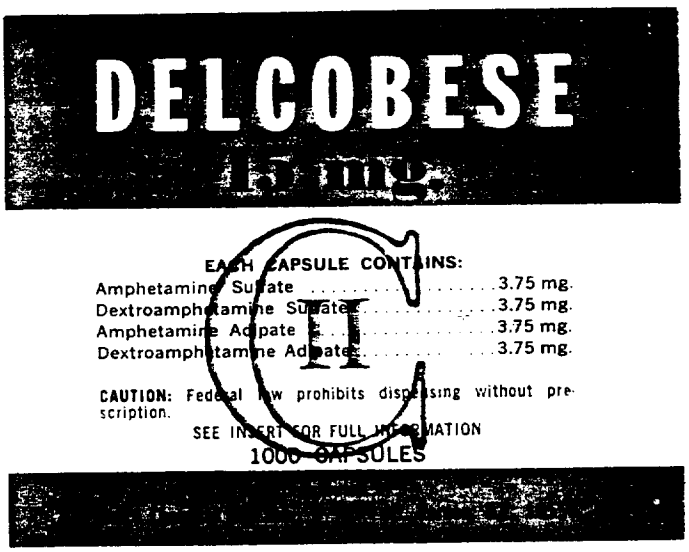
SEE INSERT FOR FULL INFORMATION

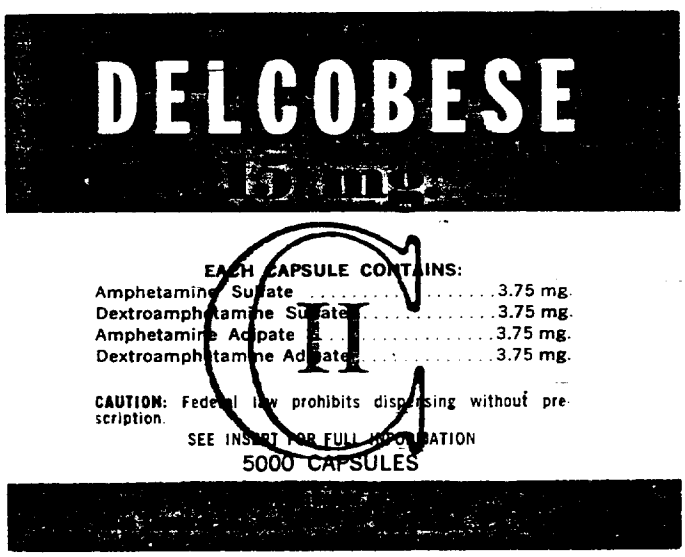
5000 CAPSULES

Distributed by
Delco Chemical Co., Inc. • Mt. Vernon, N.Y. 10550


DELCOBESE
10 mg.
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 2.5 mg.
Dextroamphetamine Sulfate ..... 2.5 mg.
Amphetamine Adipate ..... 2.5 mg.
Dextroamphetamine Adipate ..... 2.5 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
1000 CAPSULES
Delco Chemical Co., Inc. Mt. Vernon, N.Y. 10553


DELCOBESE
10 mg.
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 2.5 mg.
Dextroamphetamine Sulfate ..... 2.5 mg.
Amphetamine Adipate ..... 2.5 mg.
Dextroamphetamine Adipate ..... 2.5 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
5000 CAPSULES
Delco Chemical Co., Inc. Mt. Vernon, N.Y. 10553


DELCOBESE
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 3.75 mg.
Dextroamphetamine Sulfate ..... 3.75 mg.
Amphetamine Adipate ..... 3.75 mg.
Dextroamphetamine Adipate ..... 3.75 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
1000 CAPSULES


DELCOBESE
EACH CAPSULE CONTAINS:
Amphetamine Sulfate ..... 3.75 mg.
Dextroamphetamine Sulfate ..... 3.75 mg.
Amphetamine Adipate ..... 3.75 mg.
Dextroamphetamine Adipate ..... 3.75 mg.
CAUTION: Federal law prohibits dispensing without prescription.
SEE INSERT FOR FULL INFORMATION
5000 CAPSULES

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES

TRANSMITTAL OF PERIODIC REPORTS FOR DRUGS FOR HUMAN USE
(21 CFR 130.13, 136.35, and 146.14)

DATE SUBMITTED: Feb. 5, 1976

Form Approved Budget Bureau No. 57-R0035

INSTRUCTIONS

Submit a separate form *(parts 1 through 4-carbons intact)* for each NDA or Antibiotic Application for which the periodic report contains required reporting information. Attach two copies of report to the form.

Where the same item of information applies to more than one NDA or Antibiotic Application for preparations containing a common active ingredient, that information may be submitted as part of the report for only one such application provided all application numbers to which that part of the report applies are listed in Item 7 and provided a separate form, with duplicate copies of all other required information, is submitted for each number.

Forward form and attachments to Department of Health, Education, and Welfare, Food and Drug Administration *(MD-14)*, 200 C Street, S.W., Washington, D.C. 20204.

1. NDA NUMBER: N 8 3 5 6 4

2. REPORT NO. *(FDA Complete)*: R- 01

APPLICANT NOTE: Reference NDA and R numbers *(entered on Acknowledgment Copy)* in any subsequent correspondence regarding report.

3. CFR SECTION NUMBER *(Antibiotic only)*:

4. APPLICANT: DELCO CHEMICAL COMPANY, INC.

5. DRUG NAME: DELCOBESE CAPSULES, 5mg.,10mg., 15mg., 20mg.

6. TYPE OF REPORT *(Check one (10))*: [X] QUARTERLY [ ] SEMIANNUAL [ ] ANNUAL [ ] OTHER

7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS *(List all numbers if any part of report applies to more than one number.)*

8. PERIOD COVERED BY REPORT

FROM (11-14)		TO (15-18)	
YEAR	MONTH	YEAR	MONTH
1975	Oct. 27	1976	Jan 31

9. REPORT INFORMATION REQUIRED *(See §§ 130.13 (a) or 146.14 (a) for description)*
(Enter an "X" in Column A if you have nothing to report. Enter identification of type of information attached in Column C.)
(ALWAYS INCLUDE INFORMATION REQUIRED UNDER "d" AND "e".)

NONE A	TYPE OF INFORMATION B	(IDENTIFICATION OF TYPE OF INFORMATION ATTACHED) C
(19) X	a. CLINICAL DATA	NO MEDICAL REVIEW INDICATED SIG. date 2/20/76
(20) X	b. ADVERSE REACTION(s)	5mg. Capsules- 80 x 1M ; 64 x 5M
(21) X	c. ANIMAL DATA	10mg. Capsules-165 x 1M ; 164 x 5M
(22) X	d. CHEMICAL OR PHYSICAL DRUG PROPERTIES	15mg. Capsules-640 x 1M ; 255 x 5M
(23) X	e. MANUFACTURING OR CONTROL CHANGES (§§ 130.9 (a) (5))	20mg. Capsules-402 x 1M ; 337 x 5M
	f. CURRENT PACKAGE LABELING *(Whether or not previously submitted)*	see attached
	g. QUANTITY DISTRIBUTED	see above

Submission related to No action indicated May 26, 1976

TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT

Mario Ebanietti, Ph.D.
Executive Vice President

SIGNATURE

APPLICANTS RETURN ADDRESS *(Type within the window envelope tic marks)*

DELCO CHEMICAL COMPANY, INC.
7 MacQuesten Parkway North
Mt. Vernon, New York 10550

FDA USE ONLY

10. DATE OF RECEIPT: 24 25 26 27 28 29 — 7 6 0 2 0 9

11. REPORT FILED IN NDA NO.: 30 31 32 33 34 35 — N 8 3 5 6 4

12. DIV. CODE (38) ... TYPE CARD (80)

FDA ACKNOWLEDGMENT

RECEIVED FEB 9 1976 BUREAU OF DRUGS

FD FORM 2252 (7/68)

ORIGINAL JACKET

Orig.

- (Fold line)

- (Fold Line)

DELCOBESE

(A SINGLE ENTITY AMPHETAMINE PREPARATION)

Amphetamines have a high potential for abuse. They should thus be tried only in weight reduction programs for patients in whom alternative therapy has been ineffective. Administration of amphetamines for prolonged period of time in obesity may lead to drug dependence and must be avoided. Particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic use or distribution to others, and the drugs should be prescribed or dispensed sparingly.

Description: Delcobese is a Single entity amphetamine preparation containing the dextro and dextrolaevo isomers of Amphetamine Adipate and Amphetamine Sulfate.

Actions: Amphetamines are sympathomimetic amines wtih CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

Drugs of thls class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects, may be involved, for example.

Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short-term clinical trials.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The origins of the increased weight loss due to the various possible drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS

Narcolepsy

Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social).

Special Diagnostic Considerations:

Special etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

The characteristic signs most often observed are chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG. Learning disabilities may or may not be present. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs.

Drug treatment is not indicated for all children with MBD. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

Drug treatment is not intended for use in the child whose hyperactivity is due to environmental factors and/or primary psychiatric disorders.

Exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction, for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines (see ACTIONS) should be weighed against possible risks inherent in use of the drug, such as those described below.

CONTRAINDICATIONS

Advance arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states..

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS

When tolerance to the "anorectic" effect develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: Amphetamines have been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are alsc noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Reproduction studies in mammals at high multiples of the human dose have suggested both an embryotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: Amphetamines are not recommended for use as anorectic agents in children under 12 years of age.

SEE OTHER SIDE

PRECAUTIONS

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of amphetamines and the concomitant dietary regimen.

Amphetamines may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.

Central nervous system: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely, psychotic episodes at recommended doses.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects when amphetamines are used for other than the anorectic effect.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DOSAGE AND ADMINISTRATION

Regardless of indication, amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening medication should be avoided because of the resulting insomnia.

1. **Narcolepsy:** Usual dose 5 to 60 milligrams per day in divided doses.
2. **Minimal brain dysfunction:**
   a. Not recommended for children under 3 years of age.
   b. Children from 3 to 5 years of age: 2.5 milligrams daily, raised in increments of 2.5 milligrams at weekly intervals until optimal response is obtained.
   c. Children 6 years of age and older: 5 milligrams once or twice daily, increased in increments of 5 miligrams at weekly intervals. Only in rare cases will it be necessary to exceed a total of 40 milligrams per day.
3. **Obesity:** Usual adult dose 5 to 30 miligrams per day in divided doses.

OVERDOSAGE

Manifestations of acute overdosage with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states.

Fatigue and depression usually follow the central stimulation.

Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute amphetamine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Acidification of the urine increases amphetamine excretion. Intravenous phentolamine (Regitine) has been suggested for possible acute, severe hypertension, if this complicates amphetamine overdosage.

DOSAGE: ADULTS: Tablets or Capsules: One tablet or capsule three times a day ½ hour before meals. Third dose should be taken at 4 P.M. to avoid insomnia.

HOW SUPPLIED

Available in tablets and capsules for immediate release.

Description:

DELCOBESE
for immediate release

	5 mg.	10 mg.	15 mg.	20 mg.
Dextroamphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Dextroamphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.

In bottles of 1000's and tins of 5000's.

CAUTION: Federal Law Prohibits Dispensing without Prescription.

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	2.5 mg.
Dextroamphetamine Sulfate	2.5 mg.
Amphetamine Adipate	2.5 mg.
Dextroamphetamine Adipate	2.5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

Distributed by
Delco Chemical Co., Inc.

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	3.75 mg.
Dextroamphetamine Sulfate	3.75 mg.
Amphetamine Adipate	3.75 mg.
Dextroamphetamine Adipate	3.75 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES

NDC 697-2410-10

DELCOBESE

5 mg.

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	1.25 mg.
Dextroamphetamine Sulfate	1.25 mg.
Amphetamine Adipate	1.25 mg.
Dextroamphetamine Adipate	1.25 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

Distributed by
Delco Chemical Co., Inc. Mt. Vernon, N.Y. 10550

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

TRANSMITTAL OF PERIODIC REPORTS FOR DRUGS FOR HUMAN USE
(21 CFR 310.300, 310.302, and 431.60)

DATE SUBMITTED: August 10, 1976

Form Approved OMB No. 57-R0035

INSTRUCTIONS

Submit a separate form *(parts 1 through 4-cartons intact)* for each NDA or Antibiotic Application for which the periodic report contains required reporting information. Attach two copies of report to the form.

Where the same item of information applies to more than one NDA or Antibiotic Application for preparations containing a common active ingredient, that information may be submitted as part of the report for only one such application provided all application numbers to which that part of the report applies are listed in Item 7 and provided a separate form, with duplicate copies of all other required information, is submitted for each number.

Forward form and attachments to Department of Health, Education, and Welfare, Food and Drug Administration *(HFD-106)*, 5600 Fishers Lane, Rockville, Maryland 20852.

1. NDA OR ANDA NUMBER: N 8 3 5 6 4

2. REPORT NO. *(FDA Complete)*: R- 0 3

APPLICANT NOTE
Reference NDA and R numbers *(entered on Acknowledgment Copy)* in any subsequent correspondence regarding report.

3. CFR SECTION NUMBER *(Antibiotic only)*:

4. APPLICANT: DELCO CHEMICAL COMPANY, INC.

5. DRUG NAME: DELCOBESE CAPSULES 5mg., 10mg., 15mg., 20mg.

6. TYPE OF REPORT *(Check one (10))*: [X] QUARTERLY [ ] SEMIANNUAL [ ] ANNUAL [ ] OTHER

7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS *(List all numbers if any part of report applies to more than one number.)*

8. PERIOD COVERED BY REPORT

FROM (11-14)		TO (15-18)	
YEAR	MONTH	YEAR	MONTH
1976	May 1	1976	July 31

9. REPORT INFORMATION REQUIRED *(See §§ 310.300(a) or 431.60(a) for description)*
(Enter an "X" in Column A if you have nothing to report. Enter identification of type of information attached in Column C.)
(ALWAYS INCLUDE INFORMATION REQUIRED UNDER "f" AND "g".)

NONE A	TYPE OF INFORMATION B	IDENTIFICATION *(Volume No.(s)/Tab(s)/Page(s) of Report)* C
(19) X	a. CLINICAL DATA	Submission Noted - No Action Indicated per Letter 8/19/76
(20) X	b. ADVERSE REACTION(s)	5mg. Capsules - 73 x 1M ; 62 x 5M 383,500
(21) X	c. ANIMAL DATA	10mg. Capsules - 232 x 1M ; 129 x 5M 376,500
(22) X	d. CHEMICAL OR PHYSICAL DRUG PROPERTIES	15mg. Capsules - 555 x 1M ; 187 x 5M 1,490,500
(23) X	e. MANUFACTURING OR CONTROL CHANGES (§§ 314.8 (a) (5))	20mg. Capsules - 76 x 1M ; 298 x 5M 566,500
	f. CURRENT PACKAGE LABELING *(Whether or not previously submitted)*	see attached TOTAL: 4,315,000
	g. QUANTITY DISTRIBUTED	see above + No alone pertains gb

NOTED:
NO MEDICAL REVIEW INDICATED
SIG:
DATE: 8/19/76

TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT
Louis Cohen, President

SIGNATURE: Louis Cohen

APPLICANTS RETURN ADDRESS *(Type within the window envelope tic marks)*

DELCO CHEMICAL COMPANY, INC.
7 MacQuesten Parkway North
Mt. Vernon, New York 10550

FDA USE ONLY

10. DATE OF RECEIPT: 26 08 17

11. REPORT FILED IN NDA NO.: N 3564

12. DIV CODE (78): 1

13. TYPE CARD (80): S

14. FDA ACKNOWLEDGMENT: RECEIVED AUG 17 1976 BUREAU OF DRUGS

FORM FD 2252 (11-74)

ORIGINAL

DELCOBESE

(A SINGLE ENTITY AMPHETAMINE PREPARATION)

Amphetamines have a high potential for abuse. They should thus be tried only in weight reduction programs for patients in whom alternative therapy has been ineffective. Administration of amphetamines for prolonged period of time in obesity may lead to drug dependence and must be avoided. Particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic use or distribution to others, and the drugs should be prescribed or dispensed sparingly.

Description: Delcobese is a Single entity amphetamine preparation containing the dextro and dextrolaevo isomers of Amphetamine Adipate and Amphetamine Sulfate.

Actions: Amphetamines are sympathomimetic amines wtih CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects, may be involved, for example.

Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short-term clinical trials.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The origins of the increased weight loss due to the various possible drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS

Narcolepsy

Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social).

Special Diagnostic Considerations:

Special etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

The characteristic signs most often observed are chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG. Learning disabilities may or may not be present. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs.

Drug treatment is not indicated for all children with MBD. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

Drug treatment is not intended for use in the child whose hyperactivity is due to environmental factors and/or primary psychiatric disorders.

Exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction, for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines (see ACTIONS) should be weighed against possible risks inherent in use of the drug, such as those described below.

CONTRAINDICATIONS

Advance arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states..

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS

When tolerance to the "anorectic" effect develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: Amphetamines have been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Reproduction studies in mammals at high multiples of the human dose have suggested both an embryotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: Amphetamines are not recommended for use as anorectic agents in children under 12 years of age.

SEE OTHER SIDE

PRECAUTIONS

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of amphetamines and the concomitant dietary regimen.

Amphetamines may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

ADVERSE REACTIONS

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.

Central nervous system: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely, psychotic episodes at recommended doses.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects when amphetamines are used for other than the anorectic effect.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DOSAGE AND ADMINISTRATION

Regardless of indication, amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening medication should be avoided because of the resulting insomnia.

1. **Narcolepsy:** Usual dose 5 to 60 milligrams per day in divided doses.
2. **Minimal brain dysfunction:**
   a. Not recommended for children under 3 years of age.
   b. Children from 3 to 5 years of age: 2.5 milligrams daily, raised in increments of 2.5 milligrams at weekly intervals until optimal response is obtained.
   c. Children 6 years of age and older: 5 milligrams once or twice daily, increased in increments of 5 miligrams at weekly intervals. Only in rare cases will it be necessary to exceed a total of 40 milligrams per day.
3. **Obesity:** Usual adult dose 5 to 30 miligrams per day in divided doses.

OVERDOSAGE

Manifestations of acute overdosage with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states.

Fatigue and depression usually follow the central stimulation.

Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute amphetamine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Acidification of the urine increases amphetamine excretion. Intravenous phentolamine (Regitine) has been suggested for possible acute, severe hypertension, if this complicates amphetamine overdosage.

DOSAGE: ADULTS: Tablets or Capsules: One tablet or capsule three times a day ½ hour before meals. Third dose should be taken at 4 P.M. to avoid insomnia.

HOW SUPPLIED

Available in tablets and capsules for immediate release.

Description:

DELCOBESE
for immediate release

	5 mg.	10 mg.	15 mg.	20 mg.
Dextroamphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Dextroamphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine adipate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.
Amphetamine sulfate	1.25 mg.	2.5 mg.	3.75 mg.	5 mg.

In bottles of 1000's and tins of 5000's.

CAUTION: Federal Law Prohibits Dispensing without Prescription.

NDC 697-2410-[illegible]

DELCOBESE
5 mg.

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	1.25 mg.
Dextroamphetamine Sulfate	1.25 mg.
Amphetamine Adipate	1.25 mg.
Dextroamphetamine Adipate	1.25 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES

Distributed by

[illegible] Chemical Co., Inc. [illegible]

DELCOBESE
5 mg.

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	1.25 mg.
Dextroamphetamine Sulfate	1.25 mg.
Amphetamine Adipate	1.25 mg.
Dextroamphetamine Adipate	1.25 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES NDC 697-2410-51

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	2.5 mg.
Dextroamphetamine Sulfate	2.5 mg.
Amphetamine Adipate	2.5 mg.
Dextroamphetamine Adipate	2.5 mg.

CII

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES NDC 697-2450-10

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	2.5 mg.
Dextroamphetamine Sulfate	2.5 mg.
Amphetamine Adipate	2.5 mg.
Dextroamphetamine Adipate	2.5 mg.

CII

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	3.75 mg.
Dextroamphetamine Sulfate	3.75 mg.
Amphetamine Adipate	3.75 mg.
Dextroamphetamine Adipate	3.75 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES NDC 697-2490-10

C II

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	3.75 mg.
Dextroamphetamine Sulfate	3.75 mg.
Amphetamine Adipate	3.75 mg.
Dextroamphetamine Adipate	3.75 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES NDC 697-2490-51

C II

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

1000 CAPSULES NDC 697-2530-10

C II

DELCOBESE

EACH CAPSULE CONTAINS:

Amphetamine Sulfate	5 mg.
Dextroamphetamine Sulfate	5 mg.
Amphetamine Adipate	5 mg.
Dextroamphetamine Adipate	5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

SEE INSERT FOR FULL INFORMATION

5000 CAPSULES NDC 697-2530-51

C II

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-564

CORRESPONDENCE

Orig

Delco CHEMICAL COMPANY, INC.

RESUBMISSION
NDA ORIG AMENDMENT

7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

October 20, 1975

Marvin Seife, M.D., Director
Division of Generic Drug Monographs
Office of Drug Monographs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland, 28052

Re: Amendment to N.D.A. 83-564
Delcobese Capsules, 5 mg.,
10 mg., 15 mg., 20 mg.

Dear Dr. Seife:

Reference is made to your letter of October 17, 1975, referring to our amendment to our abbreviated new drug application #83-564, dated April 14, 1975, for Delcobese Capsules, 5 mg., 10 mg., 15 mg. and 20 mg.

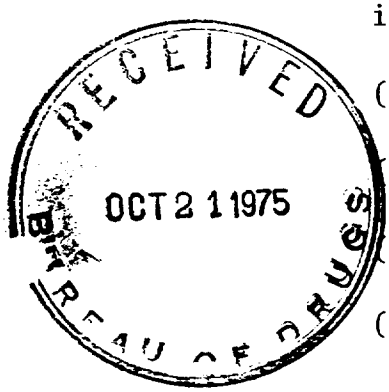
We are herewith submitting the following updated and revised information as it relates to the adequate assurance of the identity, strength, quality and purity of components and final dosage forms as requested in your above dated letter.

I. Active ingredients.

A. Page 39 of the submission - added the upper limit to the purity of the active ingredient Dextroamphetamine Sulfate not to exceed (See revised page 39 enclosed.)

B. Pages 40 and 41 of the submission - the monograph for the active ingredient d, l Amphetamine Adipate is revised to include:

(1) consolidation of pages 40 & 41 (i.e. specific rotation listed with other tests).
(2) molecular weight to read 281.34.
(3) purity limits between
(4) the addition of the specific color change in the assay titration end point to read "
(5) the addition of a Residue on Ignition test.



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CHEMICAL COMPANY, Inc.
7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

(6) identification tests for d, l amphetamine and adipate.
(See revised pages 40 and 41 enclosed.)

C. Pages 42 and 43 of the submission - the monograph for the active ingredient Dextroamphetamine Adipate is revised to include:

(1) consolidation of pages 42 and 43 (i.e. specific rotation listed with other tests).
(2) molecular weight to read 281.34.
(3) purity limits between
(4) the addition of the specific color change in the assay titration end point to read "
(5) the addition of a Residue on Ignition test.
(6) identification tests for Dextroamphetamine and Adipate.
(7) the change in Specific Rotation readings.

(See revised pages 42 and 43 enclosed.)

II. Final dosage forms.

Pages 48 and 49 of the submission - the monograph for the finished dosage form, Delcobese Capsules, is revised to include:

A. a statement of the total amphetamine base content for each dosage form.

B. the purity limits between of the labeled amount of the mixed salts or as equivalent to the amphetamine base.

C. disintegration time limits.

D. Content Uniformity test.

E. A colorimetric assay procedure using the

Delco
CHEMICAL COMPANY, Inc.
7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

he

III. Inactive Ingredients.

A. Empty Gelatin Capsules - We are submitting a specification monograph for empty Gelatin Capsules which contain statements as to its weight, identification, composition, solubility, and which also includes a statement from the capsule supplier, _____ certifying as to the capsule composition and specifications. (See Gelatin Capsules monograph and Elanco Products' letter of certification enclosed.)

The applicant has noted your request for a current description of the facilities, personnel, and standard operating procedures in use by our contract manufacturer. We refer you to pages 24 through 33 of the submitted amended application whereby the contract manufacturer, namely Inwood Laboratories, Inc., has described some current operations as it relates to Delcobese products. We have notified _____, Inc. of your suggestion to immediately review their and update those sections that require updating and will have them forward these revisions to you.

The stability program is an ongoing one and is being monitored with the proposed expiration date in mind. Any pertinent accumulated data will be submitted when available.

We trust these revisions to the specifications submitted will complete the necessary information required whereby we may be favored with an approval of the submitted application.

Sincerely yours,
DELCO CHEMICAL COMPANY, INC.

Louis Cohen
President

LC/ME

ORIG E

Delco

NDA ORIG AMENDMENT.

CHEMICAL COMPANY, Inc. FPL

7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

April 14, 1975

Marvin Seife, M. D., Director
Generic Drug Staff
Office of Scientific Evaluation
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Amendment to NDA 83-564
Delcobese Capsules, 5 mg., 10 mg.,
15 mg., & 20 mg.

Dear Dr. Seife:

Reference is made to our letter of February 7, 1975 advising you that of January 3, 1975 [illegible] Incorporated, [illegible] St., [illegible], [illegible] 11696 will be the new manufacturer for the above listed capsules and that an amended application will be forthcoming as soon as the necessary data became available.

We are herewith submitting this Amendment to our abbreviated new drug application #83-564 as set forth in paragraph 314.6 of Title 21 of the Code of Federal Regulations. This Amendment is submitted in compliance with the Federal Register notice of July 19, 1974, pages 26459/26462, reference "Drugs for Human Use - Drug Efficacy Study Implementation Certain Single Entity Oral Anorectic Drugs in Conventional or Controlled Release Dosage Forms".

Since this Amendment is substantive, the previous submission may be considered to be withdrawn and this amended application be considered resubmitted.

We trust you will find this Amendment in order.

Sincerely yours,

DELCO CHEMICAL COMPANY, Inc.

Louis Cohen

Louis Cohen, President

LC-em.

Delco

CHEMICAL COMPANY, Inc.

7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

October 24, 1975

Marvin Seife, M.D., Director
Division of Generic Drug Monographs
Office of Drug Monographs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland, 28052

Re: Amendment to N.D.A. 83-564
Delcobese Capsules, 5 mg.,
10 mg., 15 mg., 20 mg.

Dear Dr. Seife:

Reference is made to our letter of October 20, 1975. In response to your letter of October 17, 1975, referring to our amendment to our abbreviated new drug application #83-564, dated April 14, 1975, for Delcobese capsules 5 mg., 10 mg., 15 mg. and 20 mg.

In our letter of October 20, 1975, we had revised the monograph for the finished dosage form, Delcobese capsules in which the assay described therein was a colorimetric procedure using the color reaction whereby a

nt
ally

We are enclosing herewith the description of the method we used to validate this analytical procedure and trust you will find it satisfactory.

Sincerely yours,

DELCO CHEMICAL COMPANY, INC.

Louis Cohen

Louis Cohen
President

LC/MF/nc

Specializing In Obesity Products For Over 25 Years

NDA 83-564

OCT 17 1975

AF 9-389

Delco Chemical Company, Inc.
Attention: Louis Cohen
7 MacQuesten Parkway North
Mount Vernon, NY 10550

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delcobese Capsules, 5 mg., 10 mg., 20 mg.

We acknowledge your communications dated August 15, 1973, July 10, 1974 and February 7, 1975 relating to the application.

Reference is also made to your amendment dated April 14, 1975 which replaces , with Incorporated as the contract manufacturer, processor, packager and labeler of the drug dosage forms.

The application is inadequate under sections 505(b)(3) and (4) of the Act in that it fails to contain the following information required in an application:

A quantitative statement of composition of the gelatin capsules in use.
A current description of the facilities, personnel, and standard operating procedures in use by your contract manufacturer. We suggest a review of updating as necessary.

Adequate assurance of the identity, strength, quality and purity of components and final dosage forms. In this regard for:

I. Active ingredients:
   A. Dextroamphetamine sulfate: Provide for an upper purity limit as per U.S.P. standards (re: page 39, insert "....and not more than percent...."

B. d,l Amphetamine adipate:
   (1) Consolidate pages 40 and 41 (i.e. include specific rotation with other tests)
   (2) Change the molecular weight to 281.34
   (3) Change the purity limits to "....percent...."
   (4) Specify the color of the endpoint in the assay (i.e. emerald green)
   (5) Add:
      a) identification testing for the amphetamine and adipate portions of the molecule
      b) residue on ignition testing

C. Dextroamphetamine adipate:
   Appropriate comments as applied to d,l Amphetamine adipate

II. Final dosage forms:

A. Include a statement of total amine content for each dosage form.
B. Include purity specifications of not less than not more than the total established amine content.
C. Specify the disintegration time.
D. Add:
   1) identification testing for amphetamine
   2) content uniformity (total amines)

We note that stability data submitted with the application is for a period less than the proposed expiration date. Possibly you may have accumulated longer term data by this time.

Please let us have your response promptly.

Sincerely yours,

Larry Dewe 10/17/75

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

mks 10/16/75

cc:

Enter evaluation or comments for each item. If necessary, continue on 8" x 10½" paper. Key continuation to item by number. Enter "NC" if no change or "NA" if not applicable.

NDA NUMBER 83-564

25. COMPONENTS AND COMPOSITION (6, 7)

quantitative statement of composition for the gelatin capsules formulates with [illegible] of active ingredients

26. FACILITIES AND PERSONNEL (8a,b)

provided in

27. SYNTHESIS (8c)

provided in

28. RAW MATERIAL CONTROLS (8d,e)

a. NEW DRUG SUBSTANCE

inadequate for active ingredients as per issuing letter

b. OTHER INGREDIENTS

29. OTHER FIRM(s) (8i)

product is manufactured, processed, packaged and labeled by

30. MANUFACTURING AND PROCESSING (8g,h,j,k)

peovided in

31. CONTAINER (8i)

information included

32. PACKAGING AND LABELING (8l,m)

provided in

33. LABORATORY CONTROLS (In-Process and Finished Dosage Form) (8n)

inadequate for finished dosage form

34. STABILITY (8p)

additional data requested - firm provides for a 3 yr. expiration date and makes commitment to continue testing and withdraw lots that may become substandard.

35. CONTROL NUMBERS (8c)

provided in

36. SAMPLES AND RESULTS (9)

a. VALIDATION not required b. MARKET PACKAGE

37. LABELING (4)

38. ESTABLISHMENT INSPECTION

39. RECALLS

ORIG NEW CORRES

ORIG

E

Delco CHEMICAL COMPANY, Inc.

7 MacQUESTEN PARKWAY NORTH, MOUNT VERNON, NEW YORK 10550 914-664-8348

February 7, 1975

See FDA letter 10-17-75

Marvin Seife, M.D., Director
Generic Drug Staff
Office of Scientific Evaluation
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Re: NDA 83-564
Delcobese Capsules, 5mg., 10mg., 15mg., and 20mg.

Dear Dr. Seife,

Reference is made to our abbreviated new drug application dated February 23, 1973, submitted pursuant to Section (505(b) of the Federal Food, Drug and Cosmetic Act for Delcobese Capsules, 5mg., 10mg., 15mg., and 20mg.

Please be advised that as of January 3, 1975
Incorporated,
will be the new manufacturer for the above listed capsules.

We are currently collecting the necessary data required for the filing an amendment to the above numbered abbreviated new drug application and should have this necessary data available for this amendment within the next 60 days.

We trust you will find the above in order, we are

RECEIVED 1 COPY
PHOTOSTATS MADE
FOR DUP 1 TRIP 1

Sincerely yours,

DELCO CHEMICAL CO., INC.

Louis Cohen

Louis Cohen, President

RECEIVED FEB 14 1975 BUREAU OF DRUGS

LC/gf
cc: MF

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ORIG NEW CORRES

Delco CHEMICAL COMPANY, INC.

Specializing In Obesity Products For Over 25 Years

7 MacQUESTEN PARKWAY NORTH • MOUNT VERNON, NEW YORK 10550 • MOunt Vernon 4-8348

July 10, 1974

Marvin Seife, M.D., Director
Generic Drug Staff
Office of Scientific Evaluation
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref: NDA 83-564
Product: Delcobese 5mg., 10mg., 15mg., and 20 mg. capsules
"Annual Report"

Dear Doctor Seife:

There has been no significant change in our production or analytical control for our products referred to above.

We are at this time submitting our stability data for the respective dosage forms.

Respectfully submitted,
Delco Chemical Co., Inc.

Louis Cohen

Louis Cohen, Pres.

RECEIVED
JUL 16 1974
BUREAU OF DRUGS

RESUBMISSION

NDA ORIG AMENDMENT

Delco CHEMICAL COMPANY, INC.

Specializing In Obesity Products For Over 25 Years

7 MacQUESTEN PARKWAY NORTH • MOUNT VERNON, NEW YORK 10550 • MOunt Vernon 4-8348

August 15, 1973

Marvin Seife, M.D., Director
Generic Drug Staff
Office of Scientific Evaluation
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref: NDA 83-564
Product: Delcobese 5mg., 10mg., 15mg., and 20mg. Capsules

Dear Doctor Seife:

Reference is made to your communication dated August 7, 1973 - we will endeavor, herewith, to submit and clarify the requirements of the application.

I. Form 356-H-Paragraph 7. - A full statement of the composition of the drug.

a) The statement included in our submission does set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug in the form it is to be distributed-see page 1.20 of NDA.

b) The batch formulae representative of that to be employed for the manufacture of the finished dosage forms appear on Pages 1.55, 1.56, 1.57 and 1.58 of the NDA.

II. Paragraph 8 (Form 356-H)

A. "Pertaining to your role in the operations.:

[illegible] and Dextroamphetamine

[illegible] an Dextroamphetamine Adipate

III. "A more complete description of, and the data derived from studies of the stability of the drug dosage form."

Answer: We are submitting herewith stability data re the drug dosage form.

IV. "Samples of the finished capsules"

Answer: We are submitting herewith samples of the finished capsules, as per your request.

V. "Revised (1) container labels on which the statement "central stimulant short-term appetite depressant" is deleted and (2) package insert, as per the accompanying labeling guidelines and with information in the "Supplied in....." section transferred to the How Supplied section."

Answer: We are herewith submitting new labels deleting the statement "central stimulant short-term appetite depressant."

However, as to the insert guidelines you forwarded dated "Draft 1/29/73" it is not consistent with the guidelines published in the Federal Register Vol. 38 No. 28, dated Monday, February 12, 1973 which is after the Draft which you forwarded; please clarify.

Too, the "How supplied in" relates to the description of the composition of the dosage form - and we would appreciate your review of your comments in your missive dated August 7, 1973.

VI. "It is also requested that you clarify operations performed by you in connection with this application"

Answer: Delco Chemical Co., Inc. is the sole distributor of Delcobese

products and as aforementioned is in control of the synthesis of the Adipate salts of Amphetamine and Dextroamphetamine. It is under our specifications that subcontractors synthesize same.

Production for 'Delco' at is conducted under the supervision of Delco's Quality Assurance Director - Andrée R. Barresi.

[illegible] Adipate and Dextroamphetamine Adipate on pages 1-31

[illegible] sing and packing of Amphet[illegible]

[illegible] 30 [illegible] dosage form enclosed with this submission.

We would appreciate your amending our NDA accordingly, and awaiting your reply with regard to the package insert, we remain

Very truly yours,
Delco Chemical Co., Inc.

Louis Cohen

Louis Cohen, President

enc.

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper.)

1. ORGANIZATION: bd-69

2. NDA NUMBER: 83-

3. NAME AND ADDRESS OF APPLICANT (City and State)
delco chemical co., inc.
mt. vernon, ny 10550

4. DATE NDA APPROVED

5. IF PRIOR TO ... DATE APPROVED FOR EFFICACY

6. NAME OF DRUG: delcobese

7. NONPROPRIETARY NAME: adipate & sulfate salts of amphetamine + d-amphetamine

8. SUPPLEMENT NUMBER / DATE

9. PURPOSE OF SUPPLEMENT

10. AMENDMENT DATE(s): 4/6/73

11. OTHER DATE (Report)

12. PHARMACOLOGICAL CATEGORY: anorexic

13. AF NUMBER: 9-389
rexar 3-550

16. RELATED IND. NDA/M...: 83-564 = tablets

14. DOSAGE FORM: capsules

15. HOW DISPENSED: XX Rx ☐ OTC

17. POTENCY (Use): 5,10,15,20 mg.

18. NAS/NRC: ☐ UNDER REVIEW ☒ REVIEWED

19. CHEMICAL NAME

20. RECORDS AND REPORTS
CURRENT: ☐ YES ☐ NO
REVIEWED: ☐ YES ☐

21. CHEMICAL FORMULA

22. REMARKS

NOTE: 1. bioavailability deferred, as per bio committee 1/8/73
2. designation to be INADEQUATE
3. response to be requested within 120 days

23. CONCLUSIONS

inadequate letter to issue

25. REVIEWER

NAME: gmillar

SIGNATURE: [signature] 8/3/73

DATE COMPLETED: 3

DISTRIBUTION: ☒ ORIGINAL JACKET ☐ DUPLICATE JACKET ☐ REVIEWER

FDH FORM 2268 (10/65) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

Key continuation to item by number. Enter "NC" if no change or "NA" if not applicable. | 83-564

25. COMPONENTS AND COMPOSITION (6, 7)

talc used = from .in #2 capsules(specs needed)
all weight 5.5 gr.

satisfactory
note: glc assay for determination of total amphetamine

26. FACILITIES AND PERSONNEL (8e,b)

needed for (a) delco. as sponsor (b) as synthesizer of 4 active ingredients &(c) as mfg of capsules

27. SYNTHESIS (8c)

as per chemical corp:llote batch formulae given for subject ; need same for (1) [illegible]

28. RAW MATERIAL CONTROLS (8d,e)

a. NEW DRUG SUBSTANCE

[illegible] amphetamine adipate = del

(need reference for it)

b. OTHER INGREDIENTS

satisfactory

29. OTHER FIRM(s) (8f)

appropriate as per #27 & 1 labs performe certifications need , as per #30 animal studies

30. MANUFACTURING AND PROCESSING (8g,h,j,k)

need special precautions + info as to quotat as per FR of 5/8/73; otherwise = satisfavtory

Note: CII drug for batches

31. CONTAINER (8i)

in bottles of 1000 + 5000
need full information

32. PACKAGING AND LABELING (8l,m)

need full information

33. LABORATORY CONTROLS (In-Process and Finished Dosage Form) (8n)

need additional specs ts = (1)wt variation (2) (a)glc (b)non-aqueous titration for total amines.

34. STABILITY (8p)

needed

35. CONTROL NUMBERS (8c)

beeded

36. SAMPLES AND RESULTS (9)

a. VALIDATION ethod b. MARKET PACKAGE

37. LABELING (4)

revised, as per MO(jheilert)

38. ESTABLISHMENT INSPECTION

requested 8/1/73 for

39. RECALLS

na

FDH FORM 2266 (10/68)

MEMO RECORD	AVOID ERRORS PUT IT IN WRITING	DATE 2/1/73
FROM: gerry millar (thru Jack L. Meyer)		OFFICE BD-60
TO: Mr.C.G Broker (thru: Stan Stringer BD-100)		DIVISION BD-340

SUBJECT: Collaborative draft(s)

SUMMARY In connection with NDAs 83-563 for delcobese(4 amphetamine combo) tablets + capsules
83-564 5,10,15 & 20 mg.

The applicant: delco chemical co., inc
mt. vernon, ny 10550

AF: 9-389

We acknowledge receipt on 2/5/73

of abbr nda

dated 2/23/73

for the preparations

In accordance with the 2/27/73 directive, Office of Compliance a request is made for:

REQUESTED

XXX ◯ 1. establishment inspection report on

XX ☐ a. the applicant

XXXX ☐ b. others firm that mfg et al these preparations

582

◯ 2. evaluation of compliance with CGMPR

◯ 3. recommendation for approval/disapproval of the application/communication/supplement based on your evaluation of compliance with CGMPR

NOTE: have inspectors check rexar's quota, as per FR of 5/[illegible]/73

PLEASE INITIATE

SIGNATURE | DOCUMENT NUMBER

	5mg	10 mg	15 mg	20 mg
amphetamines	as per label contents			
corn starch lactose talc				

Original E

NDA ORIG AMENDMENT

Delco CHEMICAL COMPANY, INC. FPLI

Specializing In Obesity Products For Over 25 Years

7 MacQUESTEN PARKWAY NORTH • MOUNT VERNON, NEW YORK 10550 • MOunt Vernon 4-8348

PERSONALLY SUBMITTED BY
Joseph Bertolini
Rec'd by Bureau
4-12-73

April 6, 1973.

Marvin Seife, M.D., Director
Division of Actions Implementation
Drug Effecacy Study Implementation
Project Office
Bureau of Drugs, Food and Drug Administration
5600 Fishers Lane,
Rockville, Maryland 20852

Ref: NDA 83-564
Products: DELCOBESE CAPSULES, 5mg., 10 mg., 15 mg., and 20 mg.

Dear Doctor Seife:

Pursuant to Section 505(b) of the Federal Food, Drug and Cosmetic Act; and in accordance to s.s. 130.7 we are amending our New Drug Application as follows:

Under Paragraph 4 (Copies of labels) Form 356-H

We have revised the package insert; and now are submitting the new copy pertaining thereto.

Enclosed are 12 copies of the new package insert.

CEIVED 1 COPY
OTOCOPIES MADE
IR DUP TAP

RECEIVED
APR 12 1973
BUREAU OF DRUGS

Respectfully submitted,
DELCO CHEMICAL CO., INC.

Louis Cohen

Louis Cohen, President

LC:g

NDA 83-564
AF 9-389

MAR 30 1973

Delco Chemical Co., Inc.
Attention: Mr. Louis Cohen
7 N. Macquesten Parkway
Mt. Vernon, New York 10550

Gentlemen:

Reference is made to your abbreviated new drug application dated February 23, 1973, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delcobese Capsules, 5 mg., 10 mg., 15 mg., and 20 mg.

Since no provision has been made for this preparation as a sustained release capsule to be filed as an abbreviated new drug application in any Federal Register notice, the application as submitted will not be reviewed at this time.

However, the material submitted is being retained in our file.

Sincerely yours,

Marvin Seife 3/30/73

Marvin Seife, M.D.
Director
Division of Antibiotic Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NYK-DO

3/29/73

ACK.

NDA 83-564/S-001

DEC 19 1975

Delco Chemical Company, Inc.
Attention: Louis Cohen
3 MacQuesten Parkway North
Mount Vernon, NY 10550

Gentlemen:

We acknowledge receipt on November 26, 1975, of a communication of November 14, 1975, submitted on your behalf by your manufacturing facility, [redacted] is regarded as a supplemental new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delcobese Tablets, 5 mg., 10 mg., 15 mg., and 20 mg. Capsules

The supplemental application provides for control revisions at the Facility.

We have completed the review of this supplemental application and it is approved. Our letter of October 24, 1975, detailed the conditions relating to the approval of this application.

The material submitted is being retained in the file.

Sincerely yours,

Marvin Seife 12/18/75

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

5.1 .

ANDA

83-564 Amphetamine Sulfate Capsules USP, 5 mg, 10 mg and 20 mg
83-563 Amphetamine Sulfate Tablets USP, 5 mg, 10 mg and 20 mg

Lemmon Company
Attention: Stanley Scheindlin, D.Sc.
650 Cathill Road
Sellersville, PA 18960

MAR 23 1993

Dear Sir:

We acknowledge the receipt of your communications dated February 24, 1993, requesting withdrawal of approval of your abbreviated new drug applications for the above referenced products.

In compliance with your request and in accordance with Section 314.150(c) of the Regulations under the Federal Food, Drug and Cosmetic Act, action will be taken to withdraw approval of the applications. Appropriate notice will be given by publication in the Federal Register in accordance with Section 314.152.

These withdrawals will not prejudice any future filing of the applications. You may request that the information in these applications be considered in connection with any resubmission.

Sincerely yours,

Ken Johnson for

3-21-93

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

LEMMON

LEMMON COMPANY
650 Cathill Road
Sellersville, PA 18960
Phone: (215) 256-8400
Fax: (215) 721-9669

Stanley Scheindlin, D.Sc.
Director, Regulatory Affairs

3.1

WITHDRAWN

February 24, 1993

Roger L. Williams, M.D.
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA 83-564
AMPHETAMINE SULFATE CAPSULES (DELCOBESE), 5, 10, 15 and 20 mg

Dear Dr. Williams:

Manufacture and commercial distribution of this product have been discontinued for several years, and future production is not anticipated. We hereby request to withdraw the above-referenced Abbreviated New Drug Application without prejudice to any future filing.

Yours very truly,

Stanley Scheindlin

SS/cs

ORIGINAL